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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/528,644	03/20/2000	Lars Thim	3951.224-US	5698

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[REDACTED] EXAMINER

ROMEO, DAVID S

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1647

DATE MAILED: 03/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/528,644	THIM ET AL.
	Examiner	Art Unit
	David S Romeo	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 31 December 2001.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 27-39 is/are pending in the application.

4a) Of the above claim(s) 34,35,37 and 38 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 27-33,36 and 39 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) 27-39 are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) Z .	6) <input type="checkbox"/> Other: _____ .

DETAILED ACTION

The amendment filed 12/31/2001 (Paper No. 8) has been entered. Claims 27-39 are pending. Claims 34, 35, 37, 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5. Claims 27-33, 36, 39 are being examined. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

Maintained Formal Matters, Objections, and/or Rejections:

The application is not fully in compliance the sequence rules, 37 C.F.R. § 1.821-1.825.

15 The specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. A sequence is disclosed at page 13, line 28, without the appropriate sequence identifier, i.e. SEQ ID NO:. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as “residues 14 to 243 of SEQ ID NO:23” is permissible and the fragment need not be separately presented in the “Sequence Listing.”

20 Correction is required.

Claim Rejections - 35 USC § 112

Claims 27-33, 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5 The rejection of record is applied to claim 39 because stringency varies according to the hybridization conditions and the particular hybrid under study and the limitation “high stringency conditions” does not add further, meaningful structural limitations to the claimed invention.

Applicant argues that the claimed polypeptides now possess a common structural attribute, that the presence of two trefoil domains provides a common structural attribute that distinguishes the claimed polypeptide, that it is the trefoil domain structure that confers spasmolytic activity, and that the specification provides a representative number of homologues. Applicants arguments have been fully considered but they are not persuasive.

The scope of the claim includes numerous structural variants, and the genus is highly variant because the term “homologue” does not provide further, meaningful structural limitations to the claimed invention, as discussed in the last Office action; because the trefoil domain is made up of 38 or 39 amino acid residues (the present specification at page 1, full paragraph 2) and the limitation “comprising at least six disulfide bonds that form two trefoil domains” sets forth only minimal structural limitations, i.e. at least six disulfide bonds, and at the same time encompasses any and all structures that achieve the desired activity, i.e. form a trefoil domain. Nor does the limitation “at least six disulfide bond” set forth the required configuration of the disulfide bonds. The homologues at page 5, lines 6-20, are in regard to providing one or more

additional glycosylation sites and are not commensurate with the scope of the claim and the claim is not limited to homologues with one or more additional glycosylation sites.

Claim Rejections - 35 USC § 103

5 Claims 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Onda (n6) in view of Tomasetto (2, cited by Applicants), Alberts (u6), Hitzeman (x6), and Lodish (w6).

The rejection of record is applied to claim 39 because insofar as the amino acid sequence of Tomasetto's encoded protein minus the putative signal peptide is identical to Applicants' SEQ ID NO:1 and a nucleic acid molecule encoding Tomasetto's encoded protein is also a nucleic acid molecule encoding Applicants' SEQ ID NO: 1, then Tomasetto's encoded protein is encoded by a nucleic acid molecule that would hybridize to a nucleic acid molecule encoding SEQ ID NO: 1.

Applicants argue that the rejection is based upon hindsight reconstruction, that the skilled artisan would not have been particularly directed to select yeast as an expression system because 15 Onda also teaches the use of non-yeast host cells, and that hSP could have been produced by chemical means because it is a small and simple polypeptide. Applicants arguments have been fully considered but they are not persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based 20 upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In*

Art Unit: 1647

re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Onda is evidence that bacteria, yeast, and animal cells were known host cells in the art of recombinant expression of trefoil peptides, which is strong evidence of obviousness for the use of yeast as a host cell for the expression of trefoil polypeptides. An express suggestion to use yeast cells instead of non-yeast cells is not necessary to render the use of yeast cells obvious. Onda's art recognized suitability of yeast for recombinant expression of spasmolytic polypeptides supports a *prima facie* obviousness determination. The fact that other techniques for making hSP could have been used does not render the use of yeast nonobvious.

Applicants argue that it could not be predicted that expression in yeast would result in the requisite glycosylation, that at the time of Applicants' invention there was no knowledge that hSP might be glycosylated, that Onda's does not provide any guidance as to whether expression in yeast of hSP would result in properly folded and glycosylated hSP because Onda's polypeptide has only one trefoil domain and contains no putative N-linked glycosylation site. Applicants arguments and Aitken have been fully considered but they are not persuasive. The ability to predict that expression in yeast would result in the requisite glycosylation is immaterial to the present rejection because the requisite glycosylation would flow naturally from following the teachings of Onda regarding expression in yeast. The fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. The recitation of an additional advantage, in the present case "N-glycosylated", associated with doing what the prior art suggests does not lend patentability to an otherwise unpatentable invention. Onda's art recognized suitability of yeast for recombinant expression of spasmolytic

polypeptides supports a *prima facie* reasonable expectation of success determination for the proper folding of hSP upon expression in yeast.

Applicant argues that the higher activity of the glycosylated form is neither taught nor suggested in the prior art. Applicants arguments have been fully considered but they are not 5 persuasive. The fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

Claims 27, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Onda (n6) 10 in view of Tomasetto (2, cited by Applicants), Alberts (u6), Hitzeman (x6), and Lodish (w6) as applied to claim 27 above and further in view of Turco (v6). Applicants argue that because Onda (n6) in view of Tomasetto (2, cited by Applicants), Alberts (u6), Hitzeman (x6), and Lodish (w6) do not teach or suggest a glycosylated hSP the claimed pharmaceutical composition is nonobvious. Applicants arguments have been fully considered but they are not persuasive. 15 For the reasons discussed above Onda (n6) in view of Tomasetto (2, cited by Applicants), Alberts (u6), Hitzeman (x6), and Lodish (w6) teach or suggest a glycosylated hSP.

Double Patenting

Claims 27-33, 36 are rejected under the judicially created doctrine of obviousness-type 20 double patenting as being unpatentable over claims 1-8, 10-13 of U.S. Patent No. 5,783,416 (a6).
The rejection of record is applied to claim 39.

It is acknowledged that Applicants intend to submit a terminal disclaimer when the present application is allowable.

New formal matters, objections, and/or rejections:

5

Claim Rejections - 35 USC § 112

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is indefinite over the recitation of “high stringency conditions” because

10 stringency varies according to the hybridization conditions and the particular hybrid under study.
The specification fails to precisely define "stringent conditions". Any degree of stringency is
embraced by the claims. One of ordinary skill in the art would not be reasonably apprised of the
metes and bounds of the invention.

Claims 27-33, 36, 39 are indefinite because they recite the term "homologue". Because
15 the instant specification does not identify that material element or combination of elements
which is unique to, and, therefore, definitive of "homologue" an artisan cannot determine what
additional or material functional limitations are placed upon a claim by the presence of this
element.

20

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

5 MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, 10 however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

15 IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306

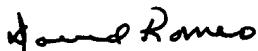
AFTER FINAL (703) 872-9307

20 IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL 25 OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED 30 TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 15, 2002